

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**  
**PATENT**

Applicant : Donovan, Stephen )  
Serial No.: to be assigned )  
(Parent App. 09/489,667) ) Examiner:  
(Parent App. C. Kam, Ph.D.)  
Filed : herewith ) Group Art Unit:  
(Parent App. January 19, 2000 ) (Parent App. 1653)  
For : CLOSTRIDIAL TOXIN )  
DERIVATIVES AND METHODS )  
FOR TREATING PAIN )

Box New App Fee  
Assistant Commissioner for Patents  
Washington, D.C. 20231

**PRELIMINARY AMENDMENT**

Dear Sir:

Please amend the subject application as follows:

**In the Specification:**

Please insert the following paragraph before the paragraph beginning at page 1, line 13:

This application is a divisional application of U.S. Serial No. 09/489,667, filed January 19, 2000, the content of which in its entirety is incorporated by reference into the present application.

Applicant: Stephen Donovan  
Serial No.: to be assigned  
Filed: herewith  
Page 2 of 13

**In the Claims:**

Please cancel claims 1-20, 26-35, and 38-66 without prejudice.

Applicant reserves the right to pursue the subject matter of these claims in a related application in the future at Applicant's discretion.

Please add claims 67-80 as follows:

67. (new) A method for obtaining an agent for alleviating pain, the method comprising:
  - (a) producing a genetic construct having codes for a clostridial neurotoxin component;
  - (b) incorporating the construct into a host organism;
  - (c) expressing the construct to produce the clostridial neurotoxin component; and
  - (d) covalently attaching the clostridial neurotoxin component to substance P.
68. (new) The method of claim 67, further comprising covalently attaching at least one spacer component between the clostridial neurotoxin component and substance P.
69. (new) The method of claim 67, wherein the clostridial neurotoxin component is produced by an organism selected from the group consisting of Clostridial beratti, Clostridial butyricum, Clostridial botulinum, and Clostridial tetani.

Applicant: Stephen Donovan  
Serial No.: to be assigned  
Filed: herewith  
Page 3 of 13

70. (new) The method of claim 67, wherein the clostridial neurotoxin component is a botulinum toxin selected from the group consisting of serotype A, serotype B, serotype C1, serotype D, serotype E, serotype F, and serotype G.

71. (new) The method of claim 67, wherein the clostridial neurotoxin component is botulinum toxin serotype A.

72. (new) The method of claim 67, wherein the clostridial neurotoxin component comprises an H<sub>N</sub> and an L chain.

73. (new) The method of claim 72, wherein the H<sub>N</sub> is produced by an organism selected from the group consisting of Clostridial beratti, Clostridial butyricum, Clostridial botulinum, and Clostridial tetani.

74. (new) The method of claim 72, wherein the L chain is produced by an organism selected from the group consisting of Clostridial beratti, Clostridial butyricum, Clostridial botulinum, and Clostridial tetani.

75. (new) The method of claim 72, wherein the H<sub>N</sub> is obtained from a botulinum toxin selected from the group consisting of botulinum toxin serotype A, serotype B, serotype C1, serotype D, serotype E, serotype F, and serotype G.

Applicant: Stephen Donovan  
Serial No.: to be assigned  
Filed: herewith  
Page 4 of 13

76. (new) A method for obtaining an agent for alleviating pain, the method comprising:

- (a) producing a genetic construct having codes for botulinum toxin;
- (b) incorporating the construct into a host organism;
- (c) expressing the construct to produce the botulinum toxin; and
- (d) covalently attaching the botulinum toxin to substance P.

77. (new) A method for obtaining an agent for alleviating pain, the method comprising:

- (a) producing a genetic construct having codes for a botulinum toxin serotype A;
- (b) incorporating the construct into a host organism;
- (c) expressing the construct to produce the botulinum toxin serotype A; and
- (d) covalently attaching the botulinum toxin serotype A to substance P.

Applicant: Stephen Donovan  
Serial No.: to be assigned  
Filed: herewith  
Page 5 of 13

78. (new) A method for obtaining an agent for alleviating pain, the method comprising:

- (a) producing a genetic construct having codes for a botulinum toxin, wherein the portion encoding an Hc of the toxin has been removed;
- (b) incorporating the construct into a host organism;
- (c) expressing the construct to produce the botulinum toxin; and
- (d) covalently attaching the botulinum toxin to substance P.

79. (new) A method for obtaining an agent for treating pain, the method comprising:

- (a) producing a genetic construct having codes for (1) a clostridial neurotoxin component and (2) substance P;
- (b) incorporating the genetic construct into a host organism; and
- (c) expressing the genetic construct to obtain a fusion protein comprising the clostridial neurotoxin component covalently coupled to the substance P.

80. (new) The method of claim 79, wherein the genetic construct includes genetic codes that encode for a spacer component between the clostridial neurotoxin component and substance P.

Applicant: Stephen Donovan  
Serial No.: to be assigned  
Filed: herewith  
Page 6 of 13

**Support for the Claims:**

Support for claim 67 may be found in the specification at page 30, lines 4-22; and in claims 21 and 25.

Support for claim 68 may be found in the specification at page 30, lines 15-16 and 20-22; and in claim 22.

Support for claim 69 may be found in the specification at page 15, lines 19-21.

Support for claim 70 may be found in the specification at page 15, lines 23-24.

Support for claim 71 may be found in the specification at page 15, lines 23-24.

Support for claim 72 may be found in the specification at page 29, lines 18-30.

Support for claim 73 may be found in the specification at page 29, lines 21-27.

Support for claim 74 may be found in the specification at page 22, line 30 to page 23, line 13.

Support for claim 75 may be found in the specification at page 22, line 30 to page 23, line 13.

Applicant: Stephen Donovan  
Serial No.: to be assigned  
Filed: herewith  
Page 7 of 13

Support for claim 76 may be found in the specification at page 17, lines 8-10; and in claims 21 and 66.

Support for claim 77 may be found in the specification at page 17, lines 8-10; and in claims 21 and 66.

Support for claim 78 may be found in the specification at page 17, lines 10-15.

Support for claim 79 may be found in the specification at page 30, lines 4-22; and in claims 23 and 25.

Support for claim 80 may be found in the specification at page 30, lines 15-16 and 20-22; and in claim 22.

**Remarks**

The amendment to the specification simply addresses the priority claim of the instant application. The parent application, U.S. Serial No. 09/489,667, is relied on for an earlier effective filing date under 35 U.S.C. § 120. No new matter has been added.

Applicant has canceled claims 1-20, 26-35, and 38-66, as set forth above. Applicant has added claims 67-80, as set forth above. Accordingly, claims 21-25, 36, 37, and 67-80 are currently pending.

Applicant: Stephen Donovan  
Serial No.: to be assigned  
Filed: herewith  
Page 8 of 13

The currently pending claims correspond to the claims of Group II as set forth in the Restriction Requirement dated December 20, 2000 in the related parent application, U.S. Serial No. 09/489,667.

Claims 67-80 are directed to methods of making the agents claimed in claims 69-80 that were filed in the parent application, U.S. Serial No. 04/489,667, in the Amendment dated April 20, 2001. The Examiner of the parent application has indicated that claims 69-80 of the parent application are allowed in the Office Action dated July 11, 2001.

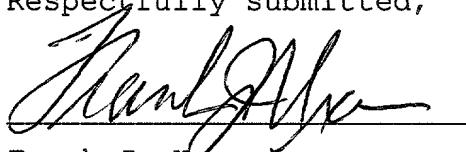
Applicant respectfully submits that the currently pending claims are in condition for allowance.

Applicant: Stephen Donovan  
Serial No.: to be assigned  
Filed: herewith  
Page 9 of 13

If a telephone interview would be of assistance in advancing prosecution of the subject application, Applicant's undersigned representative invites the Examiner to telephone either Quan Nguyen or Greg S. Hollrigel, Ph.D., at the number provided below.

Respectfully submitted,

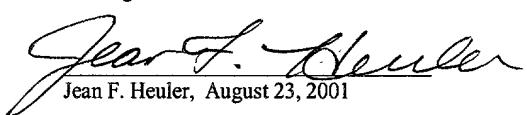
Date: August 23, 2001



Frank J. Uxa  
Attorney for Applicant  
Registration No. 25,612  
4 Venture, Suite 300  
Irvine, California 92618  
(949) 450-1750  
(949) 450-1764 Facsimile

**CERTIFICATE OF MAILING**

I hereby certify that this correspondence is being deposited with the United States Postal service as first class mail in an envelope addressed to:  
Commissioner for Patents  
Washington, D. C. 20231  
On August 23, 2001.



Jean F. Heuler, August 23, 2001

Applicant: Stephen Donovan  
Serial No.: to be assigned  
Filed: herewith  
Page 10 of 13

**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**In the Specification:**

The following paragraph has been inserted before the paragraph beginning at page 1, line 13:

This application is a divisional application of U.S. Serial No. 09/489,667, filed January 19, 2000, the content of which in its entirety is incorporated by reference into the present application.

**In the Claims:**

Claims 1-20, 26-35, and 38-66 have been canceled.

Claims 67-80 have been added as follows:

67. (new) A method for obtaining an agent for alleviating pain, the method comprising:

- (a) producing a genetic construct having codes for a clostridial neurotoxin component;
- (b) incorporating the construct into a host organism;
- (c) expressing the construct to produce the clostridial neurotoxin component; and
- (d) covalently attaching the clostridial neurotoxin component to substance P.

Applicant: Stephen Donovan  
Serial No.: to be assigned  
Filed: herewith  
Page 11 of 13

68. (new) The method of claim 67, further comprising covalently attaching at least one spacer component between the clostridial neurotoxin component and substance P.
69. (new) The method of claim 67, wherein the clostridial neurotoxin component is produced by an organism selected from the group consisting of Clostridial beratti, Clostridial butyricum, Clostridial botulinum, and Clostridial tetani.
70. (new) The method of claim 67, wherein the clostridial neurotoxin component is a botulinum toxin selected from the group consisting of serotype A, serotype B, serotype C1, serotype D, serotype E, serotype F, and serotype G.
71. (new) The method of claim 67, wherein the clostridial neurotoxin component is botulinum toxin serotype A.
72. (new) The method of claim 67, wherein the clostridial neurotoxin component comprises an H<sub>N</sub> and an L chain.
73. (new) The method of claim 72, wherein the H<sub>N</sub> is produced by an organism selected from the group consisting of Clostridial beratti, Clostridial butyricum, Clostridial botulinum, and Clostridial tetani.
74. (new) The method of claim 72, wherein the L chain is produced by an organism selected from the group consisting

Applicant: Stephen Donovan  
Serial No.: to be assigned  
Filed: herewith  
Page 12 of 13

of Clostridial beratti, Clostridial butyricum, Clostridial botulinum, and Clostridial tetani.

75. (new) The method of claim 72, wherein the  $H_N$  is obtained from a botulinum toxin selected from the group consisting of botulinum toxin serotype A, serotype B, serotype C1, serotype D, serotype E, serotype F, and serotype G.

76. (new) A method for obtaining an agent for alleviating pain, the method comprising:

- producing a genetic construct having codes for botulinum toxin;
- incorporating the construct into a host organism;
- expressing the construct to produce the botulinum toxin; and
- covalently attaching the botulinum toxin to substance P.

77. (new) A method for obtaining an agent for alleviating pain, the method comprising:

- producing a genetic construct having codes for a botulinum toxin serotype A;
- incorporating the construct into a host organism;
- expressing the construct to produce the botulinum toxin serotype A; and
- covalently attaching the botulinum toxin serotype A to substance P.

Applicant: Stephen Donovan  
Serial No.: to be assigned  
Filed: herewith  
Page 13 of 13

78. (new) A method for obtaining an agent for alleviating pain, the method comprising:

- (a) producing a genetic construct having codes for a botulinum toxin, wherein the portion encoding an Hc of the toxin has been removed;
- (b) incorporating the construct into a host organism;
- (c) expressing the construct to produce the botulinum toxin; and
- (d) covalently attaching the botulinum toxin to substance P.

79. (new) A method for obtaining an agent for treating pain, the method comprising:

- (a) producing a genetic construct having codes for (1) a clostridial neurotoxin component and (2) substance P;
- (b) incorporating the genetic construct into a host organism; and
- (c) expressing the genetic construct to obtain a fusion protein comprising the clostridial neurotoxin component covalently coupled to the substance P.

80. (new) The method of claim 79, wherein the genetic construct includes genetic codes that encode for a spacer component between the clostridial neurotoxin component and substance P.